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C-Reactive protein levels before and after non-surgical periodontal treatment in pregnant women with gingivitis and periodontitis.

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Abstract:
Background*: Periodontal disease is one of the pathologies with the highest incidence in the population, increasing with age and with greater manifestation in pregnant women due to hormonal changes that occur during pregnancy, contributing to the increase of aerobic and anaerobic bacteria in the oral cavity. The American Academy of Periodontology (AAP) has published a review of various systemic diseases where the presence of periodontal disease could be a potential risk factor. C-reactive protein (PC-R) is the ideal method for establishing an association of periodontal disease and systemic diseases. According to the official AAP guide, the purpose of periodontal therapy is to preserve the natural dentition, to maintain and improve periodontal health, comfort, aesthetics, function and provide replacements where indicated. The objective of the study is to determine the levels of C-Reactive protein before and after non-surgical periodontal treatment in pregnant women with gingivitis and periodontitis.*
Materials and Methods*: The sample was composed of 32 volunteer pregnant women, registered and evaluated in the Stomatology Service of the National Maternal Perinatal Institute (NMPI) in the city of Lima, Peru. And, they were divided into three groups according to clinical diagnosis of gingivitis, localized and generalized periodontitis. We measured before and after non-surgical periodontal treatment: gingival bleeding (% of sites) and simplified oral hygiene in the study population. And, the level of clinical insertion (CAL) and depth of pocket (PD) in the group with periodontitis; PC-R levels were also measured in the total population.*
Results*: It was found that the average gingival bleeding and oral hygiene are lower after phase I periodontal treatment in pregnant women with gingivitis and periodontitis ($p<0.05$). And, the post-treatment averages of CAL and PD in localized and generalized periodontitis are lower than the pre-treatment averages ($p<0.05$); greater average change in periodontal parameters (CAL and PD) was found in patients with generalized periodontitis. In addition, it was found that the levels of PC-R in post-treatment plasma are lower in pregnant women who presented gingivitis and localized periodontitis ($p<0.05$); however, in pregnant women with generalized periodontitis the decrease in PC-R levels was not statistically significant ($p>0.05$). Regarding the risk levels of PC-R for gingivitis and periodontitis, they decreased in pregnant women with gingivitis and localized periodontitis after non-surgical periodontal treatment; while in pregnant women with advanced periodontitis the percentage of high risk were the same before and after non-surgical periodontal treatment.*
Key Word*: Pregnant women, C-reactive protein, Non-surgical periodontal treatment, periodontal disease.*

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I. Introduction

Periodontitis is an inflammatory condition characterized by rupture of the periodontal ligament and subsequent formation of periodontal pockets, and also by loss of alveolar bone, often resulting in tooth loss[1]. Microbial dysbiosis has been related to the etiology and pathogenesis of periodontal disease [2,3].
Localized periodontal inflammatory responses and systemic inflammation are induced by periodontitis, by intervening in the release of inflammatory molecules[4]. Host cells release proinflammatory cytokines that incite neutrophils (PMNs) to the inflammatory site. PMNs release proteolytic enzymes that induce an oxidative burst

and the release of oxygen radicals known as reactive oxygen species (ROS). These ROS cause the destruction of microorganisms, at the same time they initiate the undesirable destruction of the periodontal tissue. [5,6]
Periodontal treatment aims to alter or eliminate the origin of microorganisms and prevent the progression of the disease, preserving the health status of people by avoiding the recurrence of periodontitis[7].
For the above and, considering the importance of periodontal therapy on the levels of C-reactive protein (PC-R), this study aims to answer the following question:

Will there be variations in C-reactive protein levels before and after non-surgical periodontal treatment in pregnant women with gingivitis and periodontitis?

II. Material And Methods

This prospective comparative study it is analytical, correlational; because it will evaluate the effects of non-surgical periodontal therapy on C-reactive protein levels in pregnant women with periodontitis and gingivitis. He was taken in pregnant women older than 20 weeks of gestation who attended prenatal control by external offices to the Odontostomatology service of the National Maternal Perinatal Institute Lima, Peru.
Study Design: interventional, prospective, comparative and longitudinal.
Study Location: this study was carried out in pregnant women who attended their prenatal care at the National Maternal Perinatal Institute (NMPI) generally in the urban area of Lima, with the mestizo race predominating; allowing to examine biological and behavioral variables with few confounding effects.
Sample size: 32 patients.
Subjects & selection method: The study population included pregnant women who attended prenatal care by external offices of the NMPI and referred to the Odontostomatology Service in day shift for oral evaluation dividing them into 3 groups according to their oral clinical diagnosis and the selection criteria in:
Group A (N=12 patients) - gingivitis;
Group B (N=9 patients) – localized periodontitis; and
Group C (N=11 patients) **–** generalized periodontitis
As a heterogeneous population, a type of non-probabilistic sampling was applied according to the following criteria:
Inclusion criteria:

1. Pregnant women > to 20 weeks of gestational age.
2. Presence greater than or equal to 20 teeth.
3. Presence of periodontal pocket greater than or equal to 4 mm.
4. Presence of clinical insertion loss greater than or equal to 5mm.

Exclusion criteria:

1. Pregnant women with the presence of dental prostheses.
2. With systemic diseases.
3. With multiple pregnancies.
4. That they do not present more than 3 prenatal controls.

Procedure methodology

All the pregnant women considered in this research signed informed consent approved by the Ethics Committee of the NMPI and registered in a data collection form that included socio-demographic characteristics, classification of periodontitis and the Ramfjord index with full mouth evaluation without including third molars. In addition, intra-examiner reliability was performed to evaluate the consistency of periodontal values, applying the intra-class correlation test with a value of 0.8, which indicates high consistency of the evaluations.

The periodontal variables were made with periodontal probe UCN probe 1-15 Hu Friedy, evaluating 6 areas per tooth (mesio-vestibular, vestibular, disto-vestibular, mesio-lingual, lingual and disto-lingual) and, periodontal pocket was considered with depth equal to or greater than 4 mm distinguishing as chronic localized periodontitis when less than 30% of the total areas are affected and generalized when more than 30% of the total areas are affected.

The clinical evaluation of gingivitis was performed in 6 teeth; 1.6, 2.1, 2.4, 3.6, 4.1 and 4.4 in which gingival inflammation was assessed in 4 gingival zones; mesial, vestibular, distal and lingual. A value of 0 to 3 was granted; 0= normal gum; 1= Mild swelling with slight color change and slight edema, without bleeding on probing; 2= Moderate inflammation with redness, edema, brightness and bleeding at the probe and, 3= Intense inflammation with redness, intense edema, ulceration and tendency to spontaneous bleeding.

The severity of gingivitis is obtained from the values of the four zones that are added together and divided by four, to obtain the value of each tooth; the sum of the values of the teeth and the division by the

number of teeth examined indicates the value of the Gingival Index: 0.1 to 1.0 = mild inflammation; from 1.01 to 2.0 = moderate inflammation and from 2.01 to 3.0 = severe inflammation.

Statistical analysis

Data was analyzed using SPSS version 21 (SPSS Inc., Chicago, IL). Descriptive analysis of the study variables was performed, then Kolgomorov Smirnoff and shapiro wilk normality test to determine the application of parametric or non-parametric tests, the average change of PC-R levels was evaluated from the baseline data using the Wilcoxon test, which tests whether the distribution of PC-R level values was significantly lower after non-surgical periodontal treatment; and for changes in clinical periodontal parameters between pre and post non-surgical periodontal treatment was evaluated by wilcoxon's sum of ranges test.

III. Result

The distribution of the study population according to sociodemographic data is shown in Table 1. Regarding chronological age, the lowest average age presented pregnant women with localized periodontitis (24.44 ± 3.97). It is observed that the majority presented a degree of secondary education in relation to the superior one (20/12); regarding marital status, stable union predominated in the study population (18 cases). Gestational age ranged from 19 to 20 weeks on average; and parity were more Primigravidas than Multigravidas (18/14).

Table 1. Presence of gingivitis and periodontitis according to sociodemographic data.

	Gingivitis (n=12)	Localized Periodontitis (n=9)	Generalized Periodontitis (n=11)
Age in years (average ± SD)	25,42 ± 7,32	24,44 ± 3,97	26;09 ± 5,77
Degree of instruction (secondary/upper)	7/5	4/5	9/2
Marital status (Stable Union/single/married)	6/4/2	7/2/0	5/4/2
Gestational age weeks (average ± SD)	19 ± 3,24	19,89 ± 5,18	20,18 ± 4,14
Parity (Primigravidas/Multigravidas)	6/6	5/4	7/4

In Table 2. To compare the mean differences in pre-treatment and post-treatment of periodontal phase I on probing bleeding as a percentage per site (BOP) and oral hygiene (IHOS-S) in the study population, the null hypothesis is raised that the pre- and post-treatment averages of gingival bleeding and oral hygiene are the same in gingivitis, localized and generalized periodontitis. The associated p-value is less than 0.05 at the significance level of 0.05 the null hypothesis is rejected; it is stated that the average gingival bleeding and oral hygiene are lower after phase I periodontal treatment in pregnant women with gingivitis and periodontitis.

Table 2. Gingival bleeding when probing and oral hygiene before and after non-surgical periodontal treatment according to gingivitis and periodontitis.

Parameters	Gingivitis			Localized Periodontitis			Generalized Periodontitis		
	Pre-treatment	Post-treatment	Average change	Pre-treatment	Post-treatment	Average change	Pre-treatment	Post-treatment	Average change
BOP (%sites)									
Medium±SD	9,72 ± 8,77	2,38 ± 1,47*****	7,34 ± 8,61	13,73 ± 9,36	4,97 ± 3,43*	8,75 ± 8,00	29,6 ± 19,0	13,7 ± 13,1*	15,9 ± 20,6
Range	1,38 - 32,05	0,69 - 5,07	0 - 30,13	1,19 - 27,38	0 - 11,31	-6,5 - 20,2	9,09 - 70,2	0,75 - 41,97	-8,3 - 58,83
IHO-S									
Medium ± SD	2,31 ± 0,73	1,72 ± 0,55*	0,59 ± 0,44	2,72 ± 0,85	1,78 ± 0,69*	0,94 ± 0,84	2,80 ± 0,90	2,21 ± 0,81*	0,58 ± 0,45
Range	1 - 3,5	1,66 - 2,83	-0,16 - 1,49	1,32 -3,82	0,50 - 2,8	-0,67 - 2,16	1,49 - 4	0,50 - 3,70	-0,17 - 1,33

*****P ≤ 0,05 Wilcoxon (intra-group comparison)

Periodontal parameters were evaluated in clinical adherence levels (CAL) and pocket depth (PD) in mm. Table 3 compares pre- and post-surgical periodontal treatment in pregnant women with periodontitis. The null hypothesis is raised that the averages of the pre- and post-treatment periodontal parameters and the average changes are the same. The p-value associated with the contrast statistic is less than 0.05; the null hypothesis is rejected. In conclusion, we can observe that the post-treatment averages of CAL in localized and generalized periodontitis (2.94 and 3.25 respectively) are lower than the pre-treatment averages (4.22 and 5.63 respectively); similarly for PD in post-treatment (2.76 in localized and generalized periodontitis) were lower than pre-treatment (4.08 in localized and 4.25 in generalized); greater average change in periodontal parameters (CAL and PD) was found in patients with generalized periodontitis.

Table 3. Periodontal parameters before and after non-surgical periodontal treatment in pregnant women with periodontitis.

Parámeters	Localized Periodontitis			Generalized Periodontitis		
	Pre-treatment	Post-treatment	Average change	Pre-treatment	Post-treatment	Average change
CAL (mm)						
Media ± SD	4,22 ± 1,09	2,94 ± 0,83*	1,27 ± 1,06	5,63 ± 0,92	3,25 ± 1,21*	2,38 ± 1,26
Range	2 – 6	2,13 – 5	-1 - 2,6	4 - 7	1 - 5,5	0,5 - 4
PD (mm)						
Media ± SD	4,08 ± 0,15	2,76 ± 0,54*	1,32 ± 0,61	4,25 ± 0,20	2,76 ± 0,36*	1,48 ± 0,38
Range	4 - 4,44	2,22 – 4	0 -2	4 - 4,68	2,27 - 3,4	0,8 - 2

*P ≤ 0,05 Wilcoxon (intra-group comparison)

Table 4 hypothesises that plasma PC-R levels are the same before and after periodontal treatment in pregnant women with gingivitis and periodontitis. The p-value associated with the contrast statistic is less than 0.05 in pregnant women with gingivitis and localized periodontitis; then, at the significance level of 0.05, the null hypothesis is rejected; however, in pregnant women with generalized periodontitis the p-value associated with the contrast statistic is greater than 0.05, it is accepted that the null hypothesis is not statistically significant; that is, the pre- and post-treatment non-surgical periodontal averages of PC-R are statistically not significant. We can observe a greater average change in THE levels of PC-R in pregnant women with localized periodontitis, followed by pregnant women with gingivitis.

Table 4. Plasma PC-R levels before and after the application of non-surgical periodontal treatment according to gingivitis and periodontitis.

	Gingivitis			Localized Periodontitis			Generalized Periodontitis		
	Pre-treatment	Post-treatment	Average change	Pre-treatment	Post-treatment	Average change	Pre-treatment	Post-treatment	Average change
PCR (mg/l) Media ± SD	3,66 ± 1,66	2,69 ± 1,38*	0,96 ± 1,00	4,94 ± 2,5	2,6 ± 1,26*	2,34 ± 2,25	4,48 ± 4,44	3,68 ± 4,20	0,79 ± 2,38
Range	0,76 - 6,93	0,80 - 6,09	-0,78 - 2,86	1,17 - 7,54	1 - 4,84	-1,77 - 5,47	0,88 - 15,7	1 - 15,6	-4,36 - 4,20
95 % CI	2,60 - 4,71	1,81 - 3,57		3,01 - 6,87	1,63 - 3,57		1,49 – 7,46	0,86 – 6,51	

*P ≤ 0,05 Wilcoxon (intra-group comparison)

Table 5 illustrates the reduction in PC-R risk levels for gingivitis and periodontitis. At the beginning of the study, pregnant women with gingivitis and localized periodontitis presented a higher percentage of high risk in PC-R levels (66.6% and 77.7% respectively); after non-surgical periodontal treatment, a reduction in high-risk levels of PC-R is observed (33.4% and 33.3% respectively); and. in pregnant women with advanced periodontitis, the percentage of high risk was the same before and after non-surgical periodontal treatment.

Table 5.Risk levels of plasma PC-R before and after the application of non-surgical periodontal treatment according to gingivitis and periodontitis.

Level of risk	Gingivitis				Localized Periodontitis				Generalized Periodontitis			
PCR	Pre-treatment		Post- treatment		Pre- treatment		Post- treatment		Pre-tratamiento		Post- treatment	
	n	%	n	%	n	%	n	%	n	%	n	%
High risk												
(>3 mg/l)	8	66,6	4	33,4	7	77,7	3	33,3	4	36,3	4	36,3
Medium-low risk												
(≤3 mg/l)	4	33,4	8	66,6	2	22,3	6	66,7	7	63,7	7	63,7

IV. Discussion

The attempt to conduct an intervention study involves the enrolment of the study subjects, which in this case presents advantages of uniformity with respect to socio-economic status and geographical location of residence. The pregnant women who go to their prenatal control at the National Maternal Perinatal Institute (NMPI) are particularly from the urban area of Lima, predominating in them the mestizo race; allowing to examine biological and behavioral variables with few confounding effects. Likewise, the decision to exclude subjects with multiple pregnancies and children less than three prenatal controls from the analysis was not to alter the results.

This study aimed to examine C-Reactive protein levels before and after non-surgical periodontal treatment in pregnant women with gingivitis and periodontitis. The women of our population become pregnant approximately at twenty years of age, in this study they were 25 years old on average, mostly primigravidas with secondary education, stable union and with gestational age between 19 to 20 weeks.

The results of this research showed that the average gingival bleeding and oral hygiene are lower after phase I periodontal treatment in pregnant women with gingivitis and periodontitis. Likewise, periodontal parameters were evaluated in levels of clinical adherence (CAL) and depth of pocket (PD) in mm pre and post non-surgical periodontal treatment in pregnant women with periodontitis, it was observed that the post-treatment averages of CAL and PD in localized and generalized periodontitis decreased compared to the pre-treatment averages; greater average change in periodontal parameters (CAL and PD) was found in patients with generalized periodontitis. Likewise, it was observed that the pre and post treatment averages of PC-R were lower after periodontal treatment, showing a significant change only in pregnant women with gingivitis and localized periodontitis.

The decrease in PC-R levels after periodontal treatment observed in this study was consistent with other studies.[8, 9] Elter JR. et al.[9] reported a significant decrease in PC-R 6 months after periodontal treatment. Al-Zahrani MS. et al.[10] assessed the effects of periodontitis on serum PC-R levels. The data showed that PC-R levels and periodontal health indices (gingival index, bleeding at probing, depth of pocket and level of clinical insertion) were significantly reduced after treatment. H. Bokhari S. et al.[11] showed that probing bleeding percentage (BOP), pocket depth (PD), and serum PC-R levels decreased after non-surgical mechanical periodontal treatment (phase I). The same results were also found by Mattila K. et al.[12], Iwamoto Y. et al.[13] y D' Aiuto F. et al.[14], although other studies, such as those of Ide M. et al.[15] y Yamazaki K. et al.[16] have not detected such effects significantly. High plasma levels of PC-R, fibrinogen, and white blood cells in patients with periodontal disease compared to healthy subjects at the periodontal level and the reduction in levels as a result of periodontal treatment support the theory that periodontitis contributes to inflammation throughout the body.[16,17] The findings of the present study support the hypothesis that control of local inflammation may induce a reduction in markers of systemic inflammation. That's why it's important to establish the potential benefits of periodontal therapy for improving systemic conditions.[18]

Decreased serum PC-R is significantly associated with periodontal treatment in terms of decreased infection, bacterial load, and periodontal inflammation associated with the assessment of clinical parameters.[19]

The present study demonstrates reduced risk levels of PC-R for gingivitis and localized periodontitis after non-surgical periodontal treatment. Recently the Centers for Disease Control and Prevention (CDC), in collaboration with the American Heart Association (AHA) have established a classification to establish an association between serum PC-R levels and the risk of cardiovascular disease.[20] This classification was developed after a systematic review of the evidence demonstrating the association between markers of inflammation (mainly PC-R) and coronary heart disease and stroke. Prospective epidemiological studies have consistently shown that PC-R levels independently predict the risk of initial coronary events and help us to have prognostic value in acute coronary syndromes.[21]

There is evidence to suggest that periodontal disease may be a potential trigger and a source of increased levels of markers of systemic inflammation.[22-25] Noack B. et al.[7] determined that PC-R plasma levels

increase in periodontitis and established that there is a relationship with the severity of periodontal disease and periodontal microflora. Dye B. et al.[26] found that generalized periodontitis and elevated P. gingivalis titer were independently associated with high PC-R levels. Coinciding with the studies of Ebersole J. et al.[27], Loos BG. et al.[28], Saito T. et al.[29] and our studio. Slade et al.[30,31] it also found elevated PC-R levels in individuals with extensive periodontal disease. Linden G. et al.[24] identified increased serum C-reactive protein levels in subjects with chronic periodontitis as well as Pitiphat W. et al.[32] y Briggs J. et al.[33]

Czerniuk M. et al.[34] found that patients with less advanced periodontal disease have a significantly faster decrease in inflammatory response compared to the group presenting with more advanced periodontal disease when serum PC-R levels are controlled both short- and long-term after acute coronary syndrome, these results are consistent with our study which does not show a significant reduction in PC-R levels in patients with generalized periodontitis, probably due to the time in which serum PC-R levels were controlled after periodontal treatment.

Sanadi R. et al.[35]evaluated serum PC-R levels in different types of inflammatory periodontal diseases such as gingivitis, periodontitis, acute periodontitis and pericoronal abscess, and also the possible association between periodontal disease and the risk of cardiovascular disease. In group I (gingivitis) the increase in serum PC-R levels were not significant, similar to the results of Norman M.et al.[36]. This could be because the inflammatory response is successfully contained within the periodontium. In group II (periodontitis), increased serum PC-R levels were not significant similar to the findings of Sibraa P. et al.[37] This is probably because many healthy sites may have had active insertion loss, and many diseased sites had inactive periodontal disease. In group III (acute periodontitis and pericoronal abscess), the increase in serum PC-R levels were statistically significant, suggesting that the degree of increase in PC-R levels in subjects with periodontitis depends on the severity of the disease, which differs with our study. Thakare K. et al.[38] showed a positive correlation between the severity of periodontal disease and the level of PC-R.

PC-R has been associated with adverse pregnancy outcomes, including preterm birth,[39] pre-eclampsia, and intrauterine growth restriction.[40] In addition, periodontal disease has been associated with increased risk of preterm birth and low birth weight.[41] Preterm birth is one of the major medical, social, and economic problems accounting for much of maternal and neonatal mortality and morbidity. Preterm infants are at high risk of death, neurodevelopmental disability, cognitive impairment, and behavioral disorders. Therefore, PC-R could be a plausible mediator of the association between periodontitis and adverse pregnancy outcomes.

Pitiphat W. et al.[42] showed that periodontitis can increase PC-R levels in pregnancy and this could mediate the association of periodontitis with adverse pregnancy outcomes. The association between PC-R and periodontitis during pregnancy may or may not be causal. Elevated PC-R can be caused by periodontal infection and inflammation. If this is the case, PC-R can amplify the inflammatory response through complement activation, tissue damage and induction of inflammatory cytokines in monocytes and can therefore mediate the relationship between periodontitis and adverse pregnancy outcomes.

V. Conclusion

Decreased levels of PC-R were observed in pregnant women with gingivitis and localized periodontitis after non-surgical periodontal treatment. The evidence reported in this study allows us to recommend follow-up studies with a larger population.

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